REMARKS

The Office Action mailed October 23, 2006 has been carefully considered and the following response prepared. Claims 3-11 and 16-22 are pending in the application.

New claims 23-25 have been added. New claim 23 is directed to the method of claim 10 wherein component b) of the composition is glutamine or a glutamine precursor. New claim 24 is directed to the formulation of claim 16 wherein component b) of the composition is glutamine or a glutamine precursor. New claim 25 is directed to a method for averting or reducing the risk of postoperative complications comprising the step of gastrointestinally administering to a surgical patient a composition comprising a) green tea extract and b) glutamine or a glutamine precursor. Support for new claims 23-25 can be found throughout the specification and in particular at page 10, lines 1-27.

At pages 2-3 of the Office Action, the Examiner rejected claims 3-11and 16-22 under 35 USC 103 as being unpatentable over Inanami et al. (Free Radic Res), Schneider et al. (U.S. Patent 5,656,608) and Jerkic et al. (Nephr Dial Trans) and further in view of Wu et al. (J. Nutr.) for the same reasons as the previous Office Action.

Applicants again traverse this rejection. Applicants respectfully submit that a *prima facie* case of obviousness has not been established with regard to claims 3-11 and 16-22 or new claims 23-25. A *prima facie* case of obviousness requires the following: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP at 2143.

Inanami et al. discloses oral administration of (-)catechin from green tea to gerbils for two weeks prior to surgery wherein the surgery induced transient focal brain ischemia. Administration of (-) catechin continued one week after surgery. The authors found that oral administration of (-) catechin protected the animals against ischemia-reperfusion-induced neuronal death.

Schneider et al. (U.S. Patent 5,656,608) disclose the use of one or more of the amino acids glycine, alanine and serine in combination with a) omega-3 polyunsaturated fatty acids; b) arginine or ornithine or pharmaceutically acceptable salt of arginine or ornithine; or c) RNA, nucleotide or nucleoside; or mixtures of one or more of a), b) and c) to prevent or minimize the effects of hypoxia-reperfusion injury. When used to minimize the effects of ischemia-reperfusion injury, column 7, lines 9-13 disclose that a dietary supplement containing the foregoing can be administered over a period of three days or longer before surgery, generally three to six days before surgery. Such supplements are disclosed at column 6, lines 21-61 as comprised of energy sources in an amount supplying from 600 to 1,000 Kcal/day. Schneider et al. does not disclose or suggest administration of green tea extract for any purpose, much less to prevent or reduce postoperative complications.

Jerkic et al. discloses administration of arginine, a NO substrate, to rats for four weeks prior to induction of acute renal failure. The authors found that arginine reduces tubular cell injury in acute post-ischemic renal failure. Jerkic et al. does not disclose or suggest administration of green tea extract for any purpose, much less to prevent or reduce postoperative complications.

Wu et al. provides a review of studies concerning the role of arginine on cardiovascular function and therapy. At page 2628, right column, Wu et al. discloses that studies using animal models suggest that arginine administration improves tissue preservation during reperfusion and increases regional blood flow in focal cerebral ischemia.

None of the cited references, alone or in any combination, disclose or suggest the methods of claims 3-11, 16-22 or new claims 23-24 of averting or reducing the risk of postoperative complications wherein a composition comprising a) green tea extract and b) at least one NO donor which is a substrate of NO synthetase, and/or one precursor of this NO donor is gastrointestinally administered to a surgical patient, wherein administration of the composition takes place less than twenty-four hours before a surgical procedure.

Applicants have surprisingly found that administration of the claimed composition to a surgical patient less than 24 hours before a surgical procedure averts or reduces the risk of postoperative complications. There is nothing in any of the cited references, alone or in any combination that suggests the claimed methods of averting or reducing the risk of postoperative

complications by gastrointestinally administering to a surgical patient a composition comprising a) green tea extract and b) at least one NO donor which is a substrate of NO synthetase, and/or one precursor of this NO donor before a surgical procedure wherein administration of the composition takes place less than twenty-four hours before a surgical procedure.

Inanami et al. discloses oral administration of (-)catechin from green tea to gerbils for two weeks prior to surgery. Schneider et al. discloses that when used to prevent or minimize the effects of hypoxia-reperfusion injury a dietary supplement can be administered over a period of three days or longer before surgery, generally three to six days before surgery. Jerkic et al. discloses administration of arginine, a NO substrate, to rats for four weeks prior to induction of acute renal failure. Wu et al. discloses that studies using animal models suggest arginine administration improves tissue preservation during reperfusion and increases regional blood flow in focal cerebral ischemia, but does not disclose when the arginine was administered. There is nothing in any of the cited references alone or in any combination that suggests the much shorter time period of less than 24 hours before a surgical procedure as recited in the methods of claims 3-11 and 16-24.

Even if, for the sake of argument, the references were properly combined, there is no suggestion or motivation to modify the cited references by adjusting the time of administration such that the composition comprising green tea extract and at least one NO donor or precursor thereof is administered less than 24 hours before a surgical procedure as alleged by the Examiner. The periods of administration of (-) catechin (Inanami et al.), dietary supplement (Schneider et al.) or arginine (Jerkic et al.), whether before surgery or after, are much longer than the period recited in claims 3-11 and 16-24. Persons skilled in the art looking to administer a composition containing the (-) catechin from Inanami et al. and dietary supplement from Schneider et al. or arginine from Jerkic et al. would be more likely to adjust the time of administration of such a composition to a longer time period before surgery than a shorter period of less than 24 hours as recited in the claimed methods. Inanami et al. administered (-) catechin for a period of two weeks prior to surgery. Both Schneider et al. and Jerkic et al. teach administration of arginine, but in Schneider et al. arginine, as part of a dietary supplement, is

administered for a period of three days or longer before surgery. In Jerkic et al. arginine is administered four weeks prior to surgery.

Based on the disclosures of the cited references, a person skilled the art would understand that arginine can reduce ischemic/reperfusion injury when given three or more days or four weeks before surgery, but would not know whether (-) catechin would produce such results at other times before surgery than the two weeks disclosed in Inanami et al.. The skilled person would thus most likely select a starting time for administration of the composition near the two weeks prior to surgery disclosed in Inanami et al. to have a better chance of obtaining a reduction in ischemia/reperfusion injury from a composition containing both components. Moreover, there is no reasonable expectation of success for adjusting the time of administration of the composition to a period less than twenty-four hours prior to surgery as asserted by the Examiner. The time periods prior to surgery shown in the cited prior art are days and weeks longer than the period recited in the claimed methods and there is no disclosure or suggestion in any of the cited references that a time period less than twenty-four hour prior to surgery would be effective.

Applicants have discovered, contrary to the combined teachings of the cited references that administration of a composition comprising a) green tea extract and b) at least one NO donor or precursor thereof less than twenty-four hours before a surgical procedure averts or reduces the risk of postoperative complications.

Additionally, there is no disclosure or suggestion in any of the references of administration of a composition comprising green tea extract and glutamine or a glutamine precursor for averting or reducing the risk of postoperative complications as claimed in new claims 23 and 24 or new claim 25.

Claims 3-11 and 16-22 and new claims 23-25 are not *prima facie* obvious in view of Inanami et al., Schneider et al. and Jerkic et al. in view of Wu et al. (J. Nutr.). For the reasons discussed above, a *prima facie* case of obviousness has not been established. Reconsideration and withdrawal of this section 103 rejection is respectfully requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Entry of new claims 23-25 is requested as these claims are also believed to be

allowable and raise no new issues. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

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Respectfully submitted,

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